IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA

NATERA, INC., Plaintiff, v. NEOGENOMICS LABORATORIES, INC., Defendant.	C.A. No. 1:23-cv-629

PLAINTIFF NATERA'S MEMORANDUM OF LAW IN SUPPORT OF ITS MOTION FOR A PRELIMINARY INJUNCTION PURSUANT TO FEDERAL RULE OF CIVIL PROCEDURE 65(A) AND 35 U.S.C. § 283

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I. INTRODUCTION

Defendant NeoGenomics Laboratories, Inc. ("NeoGenomics") has recently begun selling a personalized, tumor-informed molecular residual disease ("MRD") test for cancer monitoring called RaDaR™. But NeoGenomics did not use its own innovations as the foundation for RaDaR—it unlawfully and knowingly used Plaintiff Natera, Inc's ("Natera") proprietary technology. NeoGenomics' RaDaR test infringes Natera's U.S. Patent Nos. 11,519,035 (the "'035 Patent") and 11,530,454 (the "'454 Patent" and with the '035 Patent, the "Natera Patents"). It also directly competes with Natera's own tumor-informed MRD test, Signatera™, misappropriating a market that Natera invested hundreds of millions of dollars in building from the ground up. Natera seeks a preliminary injunction to enjoin NeoGenomics' infringement, avert the resulting irreparable harm to Natera's market share and reputation, and maintain the *status quo* during the pendency of this litigation.

The need for relief is urgent. On July 27, 2023—just days before the filing of this motion—NeoGenomics announced it had obtained Medicare coverage for RaDaR in breast cancer patients.[1] NeoGenomics also made clear that it plans to apply for additional cancer indications by the end of the year.[2] This is a game-changing development. Previously, RaDaR was available only to a small population of patients who were able and willing to pay thousands of dollars out of pocket for the test. Now, Medicare will make RaDaR

[1] *See* Ex. 1.

[2] *See id*.

accessible to millions of patients who would not have been able or willing to pay for it, and instead would have used Natera's competing Signatera test—the first bespoke MRD test available to patients and the only tumor-informed MRD test that had Medicare coverage before RaDaR. NeoGenomics now has the ability to disrupt the *status quo* and entrench itself in ill-gotten market share obtained using Natera's technology.

NeoGenomics cannot credibly dispute that its infringing RaDaR test and Natera's Signatera test are in head-to-head competition for the same consumers. NeoGenomics is irreparably harming Natera with aggressive and misleading advertisements and pre-established relationships with the medical community. NeoGenomics is urging Natera's customers to ***stop*** ordering Signatera and start ordering RaDaR instead. For example, even before it obtained Medicare coverage, NeoGenomics had misleadingly told consumers that RaDaR is "10x more sensitive than other MRD tests." Although such advertising is unsupported by any valid clinical comparisons, it substantially harms Natera's relationships with existing and potential customers, Natera's reputation, and ultimately, patients who deserve accurate and reliable tumor-informed MRD testing. RaDaR presents a unique and urgent threat to Signatera because NeoGenomics is poised to penetrate the tumor-informed MRD market quickly and effectively before this litigation is completed.

Natera spent years building the market that NeoGenomics now seeks to take by copying Natera's innovations. Natera invested hundreds of millions of dollars into developing these technologies, proving their efficacy, paving the way for Medicare and

insurance reimbursement, and nurturing their acceptance in the oncology community—not only for Signatera specifically, but also for MRD testing in general.

NeoGenomics is unlikely to stop infringing absent a Court order. Natera requests that the Court preliminarily enjoin NeoGenomics from infringing Natera's patents by using and selling RaDaR. *See* Fed. R. Civ. P. 65.

II. STATEMENT OF FACTS

A. Natera

Since 2004, Natera's mission has been to improve disease management by using information gained from a simple blood draw to detect disease early and proactively. Natera has developed novel technologies to make significant and accurate clinical assessments from the miniscule amounts of cell-free DNA ("cfDNA")[3] in a blood sample. These technologies include methods to modify cfDNA in nonconventional ways to capture information about genetic variations and use that information to guide healthcare decisions.

B. Signatera

In 2017, Natera launched Signatera, a blood-based test that monitors MRD in cancer patients, for research use only. MRD refers to the presence of a small quantity of tumor-derived nucleic acids (*e.g.*, DNA), indicative of a small amount of tumor cells left in the body after cancer treatment. Metzker Dec. ¶34. Typically, a positive response to cancer

[3] cfDNA refers to short fragments of DNA present in a patient's blood that can be used to characterize certain biological conditions. Metzker Dec. ¶36. Circulating tumor DNA, or ctDNA, is a special subset of cfDNA that originates from tumor, as opposed to normal, cells. *Id*. Both Signatera and RaDaR analyze ctDNA.

treatment coincides with a shrinking of the tumor until it is eventually undetectable through imaging or clinical examination. *Id*. However, if trace amounts of tumor cells remain, there is potential for relapse. *Id.* Signatera identifies MRD by detecting and quantifying circulating tumor DNA ("ctDNA"). *Id*. Signatera became commercially available to patients for clinical use in 2019. Moshkevich Dec. ¶7. Prior to Signatera, there was no commercially available tumor-informed test for monitoring ctDNA and MRD in patients. *Id*., ¶6.

Signatera and its underlying platform are the product of over a decade of hard work and hundreds of millions of dollars in research and development. Moshkevich Dec. ¶¶7, 11. Natera invested these resources to establish its reputation among physicians, insurers, and regulators as a company committed to sound science and robust clinical evidence. *Id*., ¶¶ 8,18; Malani Dec. ¶¶76-92, 150. These efforts are protected by a large, global IP portfolio. *Id*., ¶74.

C. Natera's Infringement Verdict Against ArcherDX and Invitae

The nascent tumor-informed MRD market for prescription and clinical use currently includes only two direct competitors to Signatera: RaDaR and the PCM™ test from ArcherDX/Invitae Corp. On January 27, 2020, Natera sued ArcherDX (and later also Invitae Corp. after it acquired ArcherDX) in Delaware District Court[4] for patent infringement relating to its competing personalized, tumor-informed MRD test called

[4] *Natera, Inc. v. ArcherDX, Inc*., 20-cv-0125-GBW (D. Del.).

Personalized Cancer Monitoring ("PCM"). On May 15, 2023, following a five-day trial, a unanimous jury found that ArcherDX/Invitae infringed patents related to the patents asserted here, and rejected all of the validity challenges raised by ArcherDx/Inivtae.[5] On June 15, 2023, Natera moved to permanently enjoin ArcherDX/Invitae from further infringement.[6] That motion is pending.

D. Natera's Patents-in-Suit

The '454 Patent, (D.I. 1-1), and the '035 Patent, (D.I. 1-2), cover and protect Signatera. The '454 Patent claims methods of preparing a plasma sample useful for detecting certain types of tumor-specific mutations. The '035 Patent claims methods for amplifying and sequencing multiple nucleic acid regions of interest in a single reaction volume.

E. Related Procedural History

On January 20, 2021,[7] and December 20, 2022,[8] Natera filed now-consolidated lawsuits in the District of Delaware against Inivata, NeoGenomics' corporate affiliate, for infringement of patents that are related to those found infringed and valid in the ArcherDX/Invitae case. The complaints accuse Inivata's InVisionFirst-Lung test, which is

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[5] *Id*., Dkt. No. 609.

[6] *Id*., Dkt. No. 621.

[7] *Natera, Inc. v. Inivata, Inc.*, 21-cv-0056-GBW, Dkt. No. 1 (D. Del. Jan. 20, 2021).

[8] *Natera, Inc. v. Inivata, Inc.*, 22-cv-1609-GBW, Dkt. No. 1 (D. Del. Dec. 20, 2022).

not a tumor-informed MRD test, and the RaDaR test of infringing patents including the '454 Patent. A motion to dismiss the complaint asserting the '454 Patent is pending,[9] and no discovery has occurred.

F. NeoGenomics' Infringing RaDaR Assay

On July 27, 2023, NeoGenomics obtained coverage for Medicare reimbursement for RaDaR in breast cancer.[10] This was a game-changer for NeoGenomics' market, now making the test widely accessible to millions of patients who otherwise could not afford it. Malani Dec. ¶39. NeoGenomics has announced that it plans to submit for Medicare coverage for at least two other indications by the end of 2023.[11]

Prior to the coverage determination, in March 2023—just months after being notified of Natera's infringement allegations against RaDaR[12]—NeoGenomics commercially launched RaDaR for clinical use. Metzker Dec. ¶¶59-70. RaDaR is founded upon Natera's inventions. *See* Metzker Dec. ¶¶81-169. NeoGenomics has marketed RaDaR in direct competition with Signatera, and disparaged Signatera by claiming, misleadingly, that RaDaR is "10x" more sensitive than other competing assays. Moshkevich Dec. ¶18.

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[9] *See* Ex. 2; Ex. 3; Ex. 4.

[10] *See* Ex 1.

[11] *See* Ex. 1.

[12] *See* fn. 6; *see also* Ex. 5, (In its 2022 Annual Report, NeoGenomics Laboratories acknowledged that Natera "filed a second patent infringement complaint on December 20, 2022 against Inivata Limited and Inivata Inc. alleging that RaDaR® minimal residual disease test infringes one patent.")

As NeoGenomics was aware, such a statement would be interpreted to implicate Signatera, which commands a major portion of the MRD testing market.

III. QUESTION PRESENTED

1. Does Natera demonstrate a reasonable likelihood of success on claims that NeoGenomics infringes the '454 and '035 Patents?

2. Does Natera satisfy the other requirements for a preliminary injunction?

IV. LEGAL STANDARD

35 U.S.C. § 283 provides a statutory right to preliminarily enjoin suspected patent infringement. *High Tech Medical Instrumentation, Inc. v. New Image Indus., Inc*., 49 F.3d 1551, 1554 (Fed. Cir. 1995). A patentee seeking a preliminary injunction must establish "that (1) it is 'likely to succeed on the merits,' (2) it is 'likely to suffer irreparable harm in the absence of preliminary relief,' (3) the 'balance of equities tips in [its] favor,' and (4) 'an injunction is in the public interest.'" *BlephEx, LLC v. Myco Indus., Inc.*, 24 F.4th 1391, 1398 (Fed. Cir. 2022) (quoting *Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008)).

V. ARGUMENT

A. Natera Is Likely To Prevail On The Merits

1. Natera Is Likely To Prove Infringement

"An assessment of the likelihood of infringement, like a determination of patent infringement at a later stage in litigation, requires a two-step analysis. 'First, the court determines the scope and meaning of the patent claims asserted … [Second,] the properly

construed claims are compared to the allegedly infringing device.'" *Oakley, Inc. v. Sunglass Hut Intern*., 316 F.3d 1331, 1339 (Fed. Cir. 2003) (citations omitted).

NeoGenomics' use of RaDaR infringes at least claims 1-6, 8, and 10-13 of the '454 Patent and claims 1, 12, and 13 of the '035 Patent ("the Asserted Claims"). 35 U.S.C. § 271(a); Metzker Dec. ¶¶81-169.[13] That infringement is demonstrated by NeoGenomics' and Inivata's public admissions, which demonstrate that RaDaR meets every element of the Asserted Claims. *Id*. For example, with respect to '454 Patent claim 1, NeoGenomics and Inivata's publications show that RaDaR involves preparing a plasma sample of a subject having cancer or suspected of having cancer and is used for detecting one or more single nucleotide variant ("SNV") mutations in the plasma sample. *Id*., ¶¶84-85. NeoGenomics also admits RaDaR performs whole exome sequencing on a tumor sample of a subject to identify a plurality of tumor-specific SNV mutations (*id*., ¶¶86-88), performs targeted multiplex amplification to amplify 10 to 500 target loci each having a different tumor-specific SNV mutation to obtain amplicons having a length of 50-150 bases, wherein the target loci are amplified together in the same reaction volume (*id*., ¶¶89-95), and sequences the amplicons and detects one or more tumor-specific SNV mutations wherein the sequencing has a depth of read of at least 50,000 per target locus (*id*., ¶¶96-98).

[13] The claim language is readily understood by a person of ordinary skill in the art in light of the claims and the specifications and does not need to be construed for purposes of this motion. Metzker Dec. ¶53. Natera reserves the right to respond to any claim construction arguments NeoGenomics may make.

With respect to '035 Patent claim 1, NeoGenomics and Inivata's publications admit that RaDaR involves amplifying and sequencing DNA (*id*., ¶¶140-141) by tagging isolated cell free DNA that is isolated from a blood sample derived from men or women with one or more universal tail adaptors (*id*., ¶¶142-148), performing targeted amplification of a plurality of loci having single-nucleotide mutations in a single reaction volume, introducing a barcode and one or more sequencing tags through amplification (*id*., ¶¶149-156), and conducting massively parallel sequencing wherein the plurality of targeted loci comprises 25-2,000 loci associated with cancer (*id*., ¶¶157-161).

Further, by encouraging and directing its corporate affiliate, Inivata, to perform the assay, with knowledge that doing so infringes, NeoGenomics induces infringement. 35 U.S.C. § 271(b); *Global-Tech Appliances, Inc. v. SEB SA*, 563 U.S. 754 (2011). NeoGenomics partnered with Inivata to commercialize RaDaR.[14] While its insurance reimbursement applications, including MolDX, list Inivata as authorized to perform RaDaR, RaDaR is ordered through NeoGenomics.[15] NeoGenomics has known that RaDaR infringes the '454 Patent at least because Natera sued Inivata for infringing it in December 2022, and NeoGenomics knew about that suit when it was filed.[16] NeoGenomics also knows about RaDaR's infringement of the '035 Patent at least as of the filing of the

[14] *See* Ex. 6.

[15] *See* Ex. 7; Ex. 8.

[16] *See* fn. 9.

complaint filed in this case. *BillJCo, LLC v. Cisco Sys., Inc.,* No. 2:21-CV-00181-JRG, 2021 WL 6618529, at *6 (E.D. Tex. Nov. 30, 2021).

2. NeoGenomics Cannot Raise A Substantial Question Concerning Patent Validity

The Asserted Claims are entitled to a presumption of validity and "the very existence of the patent satisfies the [patentee]'s burden on validity" when moving for a preliminary injunction. *Purdue Pharma L.P. v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1365 (Fed. Cir. 2001). The party opposing a preliminary injunction bears the initial burden "to come forward with evidence of invalidity." *Titan Tire Corp. v. Case New Holland, Inc*., 566 F.3d 1372, 1376 (Fed. Cir. 2009). "The ultimate question . . . is whether the challenger's evidence of invalidity is sufficiently persuasive that it is likely to overcome the presumption of patent validity." *PPG Indus., Inc. v. Guardian Indus. Corp*., 75 F.3d 1558, 1566 (Fed. Cir. 1996) (affirming preliminary injunction).

Inivata has moved to dismiss Natera's '454 Patent claims in the parallel District of Delaware proceedings based on lack of patent-eligible subject matter under 35 U.S.C. §101, but that motion is without merit for the reasons stated in Natera's Opposition.[17] Further, in the *ArcherDX* case involving patents related to the '454 and '035 Patents, the

[17] *See* Ex. 3, *Natera, Inc. v. Inivata, Inc.*, 21-cv-0056-GBW, Dkt. No. 37 (D.Del. Jan. 20, 2021). Inivata's motion to dismiss remains pending.

jury rejected the numerous invalidity defenses raised by those defendants, confirming that NeoGenomics is unlikely to invalidate Natera's related patent claims here.[18]

B. Natera Will Likely Suffer Irreparable Harm Absent A Preliminary Injunction

Now that it has obtained Medicare coverage for breast cancer, and has announced plans to submit for at least two additional indications by the end of 2023,[19] NeoGenomics is uniquely positioned to rapidly and substantially subvert Signatera's tumor-informed MRD market share. In fact, because NeoGenomics controls a critical entry point—access to cancer patients' biopsy tumor tissue—through its existing relationships with pathologists, NeoGenomics is able to convert potential Natera customers even before Natera becomes aware of a clinical opportunity. Malani Dec. ¶129. NeoGenomics' CEO recently acknowledged "the importance of pathologists, especially in MRD" to access tumor tissue, and highlighted NeoGenomics' longstanding control over the "distribution channel in the community hospitals, in particular, with pathologists."[20]

NeoGenomics is already a large pathology reference laboratory, with testing sites across the nation, that advertises itself as providing "one-stop" testing through both traditional pathology evaluations and now, tumor-informed MRD analysis using RaDaR. NeoGenomics leverages these deep channels while alleging that multiple vendors

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[18] *Natera, Inc. v. ArcherDX, Inc*., 20-cv-0125-GBW, Dkt. No. 609, No. 612 (D. Del. May 18, 2023); *Natera, Inc. v. Inivata, Inc.*, 21-cv-0056-GBW, Dkt. No. 37 (D.Del. Jan. 20, 2021).

[19] *See* Ex. 1, Malani Dec. ¶39.

[20] *See* Ex. 16, pp. 4, 16.

unnecessarily "increases complexity." Malani Dec. ¶128. Using a dual salesforce strategy that targets both pathologists and oncologists, NeoGenomics makes unfounded claims about the superiority of its RaDaR assay and thereby severs Natera's access to the market. *Id*., ¶129; Moshkevich Dec. ¶24. Absent urgent relief from the Court, NeoGenomics' infringement will continue to cause irreparable harm to Natera. *See Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922, 930–31 (Fed. Cir. 2012) (affirming a finding of irreparable harm based on "damage to [patentee's] price, reputation, and business opportunities"); *see also Douglas Dynamics, LLC v. Buyers Prods. Co.,* 717 F. 3d 1336, 1344–45 (Fed. Cir. 2013) (marketplace exclusivity "is an intangible asset that is part of the company's reputation"); *see also* Malani Dec. ¶¶183-184.

1. Natera Will Suffer Lost Market Share Without A Preliminary Injunction

There are only three personalized, tumor-informed MRD tests on the commercial market—Signatera, RaDaR, and Invitae's PCM. Malani Dec. ¶39. Natera is already seeking a permanent injunction against PCM. Only Signatera and RaDaR are covered for Medicare reimbursement.[21] The threat posed by RaDaR is immediate and requires prompt Court intervention to prevent further irreparable harm to Natera. An injunction is justified for at least the following reasons:

First, as explained above, NeoGenomics has deep channels into the oncology community that it is leveraging to capture and scale MRD testing revenue. *See* Ex. 10, p.2

[21] *See* Ex. 1; Ex. 9 at p.1.

(NeoGenomics CEO stating that "[w]e have a significant share of oncology patient testing volume in the US and one of the largest patient oncology databases"); *id*. at p.4 ("[W]e are well on our way to becoming a leading cancer testing, information and decision support company."). In many cases, NeoGenomics provides initial genetic analysis of tumor biopsy samples and has unique knowledge of initial cancer diagnoses as well as existing connections to physicians and patients that can be leveraged to lobby for MRD testing opportunities—before Natera is even aware that any such opportunity exists. Malani Dec. ¶129. Without a preliminary injunction, Natera will be forced to compete with NeoGenomics' ability to leverage such connections to drive adoption of an infringing test in a narrow market.

This danger is heightened by NeoGenomics' efforts to aggressively drive adoption of its infringing test. It has expanded and reorganized its workforce and redeployed resources to focus on RaDaR. *See*., *e.g*., Ex. 10 at p.3 ("For our second priority,…we repositioned our go-to-market approach with the successful launch of RaDaR MRD assay in four indications, breast, lung, head and neck, and colorectal. The RaDaR assay has been available over the last year for use in clinical research studies and pharmaceutical collaborations. Now it's fully available to US clinicians…. [W]e have completed the buildout of our pharma and bioinformatics salesforce teams, which positions us well for continued growth.").

It has reached out to Natera's customers to promote its RaDaR test (Moshkevich Dec. ¶24) and has also misleadingly promoted its test as "10X more sensitive" than other

tests on the market, and as "allow[ing] clinicians to identify cancer recurrence earlier." Ex. 10 at 3. It has also recently secured Medicare coverage for RaDaR in the breast cancer indication and plans to apply for approval for additional indications by year end.

"Head-to-head competition and lost market share tend to evidence irreparable harm." *TEK Glob., S.R.L. v. Sealant Sys. Int'l, Inc*., 920 F.3d 777, 793 (Fed. Cir. 2019). "Where two companies are in competition against one another," as Natera and NeoGenomics are here, "the patentee suffers the harm—often irreparable—of being forced to compete against products that incorporate and infringe its own patented inventions." *Douglas Dynamics*, 717 F.3d at 1344–45; *Broadcom Corp. v. Emulex Corp.*, 732 F.3d 1325, 1338 (Fed. Cir. 2013) ("The district court determined that Broadcom and Emulex were competitors and that Broadcom lost market share while Emulex gained it—thus Broadcom established irreparable harm.").

Natera also has *never* licensed its patents for competing personalized, tumor-informed MRD tests. Moshkevich Dec. ¶16. This unwillingness to license and direct competition with the non-movant in a limited market weighs in favor of a finding of irreparable harm. *Presidio Components Inc. v. Am. Tech. Ceramics Corp.*, 702 F.3d 1351, 1363-64 (Fed. Cir. 2012).

The personalized MRD testing market is rapidly growing, and the share of that market Natera would be entitled to if a preliminary injunction is not entered would be infeasible to determine with certainty after the fact. According to some analysts, the addressable MRD testing marketplace is expected to grow from $27 billion in 2022 to $93

billion by 2027. Malani Dec. ¶57. The wide bounds in the estimated future market size, the share that Natera would have achieved in the absence of infringement, and the profits that Natera would have accrued will be difficult and likely infeasible to determine if infringement continues through completion of discovery, trial, and entry of a final judgment.

2. Natera Will Lose Its First Mover Advantage If A Preliminary Injunction Is Not Entered

Natera revolutionized MRD and cancer recurrence detection. It created and was the first mover in the tumor-informed MRD testing market. Moshkevich Dec. ¶5. The development and commercialization of Signatera created the first product in the personalized ctDNA testing space. *Id*. at ¶6. Natera enjoys a first-mover advantage in the personalized, tumor-informed MRD testing market. Malani Dec. ¶¶134-141. But that first-mover advantage is being threatened by NeoGenomics' infringement and rapid entry into the market based on that infringement. *Id*.

The loss of the patentee's right to a "first-mover" advantage is irreparable harm from infringement. *Bio-Rad Labs., Inc. v. 10X Genomics Inc*., 967 F.3d 1353, 1378–80 (Fed. Cir. 2020). "Money damages alone cannot restore the technological lead-time that [a patentee] would have enjoyed as the technology leader in the market." *EyeTicket Corp. v. Unisys Corp*., 155 F. Supp. 2d 527, 548 (E.D. Va. 2001). Companies gain a competitive advantage by enjoying a period of exclusivity after being the first to establish a new market. Malani Dec. ¶136. That period of exclusivity facilitates the establishment of brand recognition, customer loyalty, and strong business foundations due to the cost-prohibitive

nature of switching to rival products. *Id*. ¶¶136, 141. NeoGenomics' rapid entry into the market, enabled entirely by its infringement, particularly when coupled with its unique capability to divert MRD testing revenues through its deep channels in the oncology community and its use of misleading comparisons to Signatera, has undermined and will continue to erode the benefits Natera is entitled to enjoy.

Natera is the leader in the MRD testing market. Since its launch, Signatera has received numerous awards and recognitions, including a Medtech Breakthrough Award, Breakthrough Device Designations, and Advanced Diagnostic Laboratory Test status. Malani Dec. ¶42. Natera was "first to market in monitoring colon cancer patients with a simple ctDNA-based blood test [and] has an opportunity to build a significant lead against other players," (Ex. 11 at p.8) it "has established an early lead in the $20B MRD market … both in terms of volume, reimbursement, and clinical evidence," (Ex. 12 at p.2) and enjoys a "definitive" first mover advantage (Ex. 13 at p.3). Its patent-protected head start "creates a unique competitive advantage unseen in the clinical lab industry." Ex. 14 at p.10.

To leverage that first-mover advantage, Natera invested heavily in expanding the market for its patented inventions. Third-party analysts report that Natera "is driving the trajectory of the early commercial ramp in a massive long-term growth market" and "driving early market penetration." Ex. 15 at pp.3,5; Malani Dec. ¶92. These investments "raise awareness of the power of MRD testing in general" and benefit both Natera and its infringing competitors because a "rising tide will lift all boats." Ex. 11 at p.10.

NeoGenomics is free-riding on Natera's investments, and its infringement threatens Natera's patent-protected first-mover advantage. For example, Natera has invested heavily in obtaining local coverage determinations ("LCDs") for Signatera. Malani Dec. ¶¶85-88, 150. LCDs are granted by regional Medicare Administrative Contractors. *Id*., ¶31. To obtain an LCD, Natera invested heavily in clinical validation of Signatera. *Id*., ¶¶85-88. Natera's Medicare LCDs have been identified as "a key catalyst to getting [the recurrence monitoring oncology liquid biopsy market] off the ground." Ex. 15 at p.13. Signatera's LCD and corresponding reimbursement coverage allow future market entrants (such as NeoGenomics) to have a simplified process to access reimbursement coverage. Malani Dec. ¶88. NeoGenomics is free-riding on Natera's hard-earned investments.

Due to the early stages of the tumor-informed MRD market, the damage from erosion of Natera's first-mover advantage from infringement absent an injunction would not be readily quantifiable and the total addressable market is likewise difficult to predict. *Id*. ¶¶138-139.

3. Natera Will Suffer A Loss Of Clinical Opportunities And Biopharmaceutical Partnerships If A Preliminary Injunction Is Not Entered

Opportunities to partner in clinical trials and projects with biopharmaceutical companies are a large component of MRD testing business. These opportunities are competitive and part of a cycle wherein multiple companies may vie for a partnering opportunity with the winner generating data, revenue, and credibility, thereby increasing its odds of winning additional trials. Malani Dec. ¶¶103-105; Moshkevich Dec. ¶25. *See*

Hybritech Inc. v. Abbott Labs., 849 F.2d 1446, 1456 (Fed. Cir. 1988). Winning the opportunity to partner in clinical trials allows a company to generate data necessary to achieve positive coverage determinations, insurance reimbursement, and in certain instances, can lead to approval of a test as a companion diagnostic ("CDx"),[22] all of which unlock access to the larger clinical market. Malani Dec. ¶103. Companies must, therefore, compete for and win the opportunity to partner in numerous trials, not only for short-term revenue, but also for long-term recognition and access to the clinical market. *Id*., ¶103.

NeoGenomics' infringement undermines Natera's ongoing research and development efforts. NeoGenomics' infringement has already deprived Natera of an opportunity to partner with Moderna for its PCV study in Melanoma (Moshkevich Dec. ¶25), and threatens to continue to deprive Natera of clinical opportunities and biopharmaceutical partnerships critical to Natera's business. Losing further contracts will deprive Natera of R&D opportunities, including access to rare and limited patient samples and precious clinical data made available only through biopharmaceutical partnerships with drug developers. Such opportunities allow Natera (or NeoGenomics) to improve its underlying technology to address current and new disease paradigms, to make potentially fundamental new scientific discoveries, and to secure insurance reimbursement for disease indications. Once such opportunities are lost, they are irreplaceable—the underlying cancer

[22] A CDx is a product for which the biopharmaceutical company and diagnostic company file jointly for regulatory approval of the drug and the diagnostic. Malani Dec. ¶29. For example, a CDx could determine whether a patient's tumor has a specific gene change that is the target of a corresponding cancer drug. *Id*.

tissue biopsy samples are consumed and the patients involved exit the window where MRD testing is relevant, and such studies are too prolonged and expensive to be easily repeated by the biopharmaceutical partner.

Precise and complete quantification of the harm due to NeoGenomics' infringement is not feasible. First, marketplace access is complex. Though it has announced plans to submit for Medicare coverage for at least two additional indications by the end of 2023,[23] RaDaR has not yet achieved an LCD for indications other than breast cancer, making uncertain the degree of harm Natera will suffer from NeoGenomics' infringement. Malani Dec. ¶¶48, 98-102; *see also Hybritech*, 849 F.2d at 1456 (evidence that "the potential injury is unpredictable" supported finding of irreparable harm). Indeed, NeoGenomics initially failed to gain coverage for colorectal cancer in 2022.[24] Second, due to the early stage of the market and the varying indications that are developing within it, it is uncertain how MRD testing products will be used within a given indication or between indications, in the clinical setting. *Id*. ¶¶94-97; *see also Hybritech*, 849 F.2d at 1456 (evidence that the "the field of technology covered by the . . . patent was new" supported finding of irreparable harm). Third, the estimated size of the total addressable market has very wide bounds, indicating substantial uncertainty. *Id*. ¶101.

[23] *See* Ex. 1.

[24] *See* Ex. 1.

4. Natera Will Suffer Reputational Harm If A Preliminary Injunction Is Not Entered

Harm to reputation has long been recognized as irreparable. *See Douglas Dynamics*, 717 F.3d at 1344; *Celsis*, 664 F.3d at 930. NeoGenomics' infringement harms Natera's reputation as a pioneer and leader in personalized, tumor-informed MRD testing.

The development of this nascent industry requires careful marketing supported by robust clinical evidence to foster trust and acceptance within the medical community among physicians and patients. Moshkevich Dec. ¶18. Relying on its infringing RaDaR assay, however, NeoGenomics is attempting to steal the market with unsupported and misleading clinical and superiority comparisons. *Id*. at ¶¶20-25. For example, NeoGenomics touts that its infringing RaDaR assay is "10x" more sensitive "compared to other leading MRD tests," even though there are no head-to-head studies nor appropriate clinical evidence to validate the claim. *Id*. at ¶¶21-22. NeoGenomics also promotes its infringing RaDaR test for use in colorectal cancer despite having no clinical evidence for this indication. *Id*. at ¶25.

In making these unfounded and misleading claims, NeoGenomics confuses the market, threatens the adoption of tumor-informed MRD testing, and creates the potential for distrust and backlash within the oncology community. *Id*. NeoGenomics' actions are harming not only Natera's reputation, but also the growth of the personalized tumor-informed MRD market—and ultimately patients who can benefit from this bespoke approach—that Natera has built through its commitment to robust clinical testing, cautious advertising, and building of trust.

5. There Is A Nexus Between Infringement And Irreparable Harm To Natera

For an injunction to issue, the infringing features do not need to be the "exclusive or predominant reason" to purchase the infringing products, but there must be '"some connection' between the patented features and the demand for [the accused] products." *Apple Inc. v. Samsung Elecs. Co., Ltd*, 809 F.3d 633, 642 (Fed. Cir. 2015). The patented features do not "need to drive demand, but just that they impact consumers' decisions to purchase." *Bio-Rad Labs. v. 10X Genomics*, 2019 WL 3322322, at *2-*3 (*quoting Apple,* 809 F.3d at 642). A showing that the patented technology is foundational to the infringing product establishes the required "some connection." *Id.*

There is a clear connection between NeoGenomics' infringement and Natera's irreparable harm. Natera's patents-in-suit claim methods that allow personalized, tumor-informed MRD testing to detect cancer with robust sensitivity and specificity. The infringed patent claims cover the entire RaDaR workflow and underlie its foundation. Metzker Dec., §VIII. Without infringing Natera's patents, NeoGenomics could not perform RaDaR or compete in the personalized, tumor-informed MRD test market.

C. The Balance Of Harms Tips In Favor Of A Preliminary Injunction

The third preliminary injunction factor, the balance of harms, weighs in favor of a preliminary injunction. Absent a preliminary injunction, Natera will lose the value of its patents and suffer the irreparable harms described above. *See Celsis In Vitro*., 664 F.3d at 931. Those harms are not outweighed by any arguable harm to NeoGenomics.

First, NeoGenomics has only very recently entered the personalized, tumor-informed MRD testing market, and it only did so after receiving notice of Natera's patent infringement allegations.[25] NeoGenomics, therefore, proceeded at its own risk. *See LEGO A/S v. ZURU* Inc., 799 F. App'x 823, 832 (Fed. Cir. 2020) (affirming preliminary injunction where "defendant's injuries [would] result solely from its own deliberate acts of infringement engaged in despite the fact that ... [the patentee] ... sent [the defendant] ... cease and desist letters"); *Celsis In Vitro*, 664 F.3d at 931 (affirming preliminary injunction where the defendant's "losses were the result of its own calculated risk in selling a product with knowledge of [plaintiff's] patent"). Moreover, RaDaR only launched commercially and became available to patients through physician prescription very recently in Q1 2023, and has not yet gained significant adoption. The recent grant of Medicare coverage on July 27, 2023 provides a critical impetus because it makes RaDaR widely accessible to patients and thus paves the way to significant patient uptake if no action is taken. Because NeoGenomics' presence in the market is not yet well-established and only occurred after learning of Natera's infringement allegations, the balance of hardships favors an injunction.

Second, Natera expects oncology to become its largest market and Signatera to increasingly drive its revenues. Malani Dec. ¶158. Signatera is expected to comprise more than 30% of Natera's revenue and a majority of its projected revenue growth by 2025. *Id*., ¶156. An October 2022 analyst report noted that "Natera represents the stock with the most

[25] *See* fn. 9.

exposure to MRD," but it "[does not] see MRD as a major contributor to the equity value" of NeoGenomics because RaDaR is expected to comprise only a small portion of NeoGenomics' sales. *Id*., ¶161. NeoGenomics offers multiple other products and services, including laboratory diagnostic and clinical trial services, pharmaceutical services, informatics, and patient-facing services; RaDaR is only one of numerous products offered by NeoGenomics' which did not significantly contribute to NeoGenomics' revenues in 2022. *Id*., ¶156. In short, Natera's growth is predicated on the future success of Signatera, while RaDaR likely comprises a smaller percentage of NeoGenomics' future revenues. *Id*. ¶¶159-162. *See Morris & Associates, Inc. v. Cooling & Applied Tech., Inc*., No. 5:09-cv-23-BR, 2010 WL 4484640, *10 (E.D.N.C. 2010) (balance of harms favored a preliminary injunction where the defendant had the "ready ability to sustain its business operations through the sale of its other products and services not alleged to be infringing"); *Bio-Rad*, 967 F.3d at 1379.

Third, NeoGenomics' infringement threatens Natera's investment in Signatera and its inventions. Natera has spent hundreds of millions of dollars on research and development of Signatera. Moshkevich Dec. ¶15. NeoGenomics is free riding on the groundwork that Natera has laid not only to establish Signatera as a first mover in the tumor-informed MRD market but also to establish and grow that market itself. Malani Dec. ¶¶76-92. If a preliminary injunction is not granted, NeoGenomics will continue benefiting competitively from Natera's investments, without having made such investments itself,

jeopardizing Natera's ability to gain a return on those investments and discouraging Natera from making future ones. *Id.* ¶¶150-154.

Fourth, absent an injunction, Natera will be forced to compete against its own inventions. *See Metalcraft of Mayville, Inc. v. The Toro Co*., 848 F.3d 1358, 1369 (Fed. Cir. 2017) (affirming preliminary injunction where, "in the absence of an injunction, [the patentee] would face substantial hardship in being forced 'to compete against its own patented invention'"); *Windsurfing Int'l, Inc. v. AMF, Inc.*, 782 F.2d 995, 1003 n.12 (Fed. Cir. 1986) ("requiring Bosch to compete against its own patented invention, with the resultant harms described above, places a substantial hardship on Bosch. This factor, therefore, favors entry of an injunction in this case").

D. A Preliminary Injunction Is In The Public Interest

There is a strong public policy in favor of enforcing patents that are likely valid and infringed. *See PPG Indus., Inc.* , 75 F.3d at 1567 (district court did not err in ruling that the "strong public policy favoring the enforcement of patent rights" favored granting the preliminary injunction); *Abbott Labs. v. Andrx Pharms., Inc*., 452 F.3d 1331, 1348 (Fed. Cir. 2006) ("absent any other relevant concerns, we agree with the district court that the public is best served by enforcing patents that are likely valid and infringed"). "[T]he focus of the district court's public interest analysis should be whether there exists some critical public interest that would be injured by the grant of preliminary relief." *Hybritech*, 849 F.2d at 1458. Only "in rare instances" have courts "exercised their discretion to deny

injunctive relief in order to protect the public interest." *Rite-Hite Corp. v. Kelley Co.*, 56 F.3d 1538, 1547 (Fed. Cir. 1995).

This is not such a rare case. NeoGenomics cannot demonstrate an important public need or any other "relevant concern" that outweighs the need to uphold Natera's patent rights, and any evidence of even some general public benefit from infringement would be insufficient. Signatera is clinically validated for every indication RaDaR claims to cover. Malani Dec. ¶170.[26] Further, the injunction Natera requests would permit NeoGenomics to continue to supply RaDaR for use by patients who had used it prior to entry of the injunction. *See i4i Ltd. Partnership v. Microsoft Corp*., 598 F.3d 831, 863, (Fed. Cir. 2010) (affirming injunction that "exclud[ed] users who purchased or licensed infringing . . . products before the injunction's effective date" because that carve out "greatly minimizes adverse effects on the public"). Patients that have previously used RaDaR will, therefore, not be prevented from using it.

Natera also has the capacity to meet future demand and the ability to increase its capacity. Malani Dec. ¶¶174-182. *See Metalcraft of Mayville*, 848 F.3d at 1369 (affirming finding that public interest favored an injunction where the patented invention would remain available from the plaintiff); *Celsis*, 664 F.3d at 931-32 (public interest supported

[26] Although NeoGenomics claims RaDaR is superior to Signatera, Natera disputes that assertion (*see* Moshkevich Dec. ¶¶21-22; Metzker Dec. ¶47) and, even if it were true, it would not tip the public interest against an injunction. *See Acumed LLC v. Stryker Corp*., 551 F.3d 1323, 1331(Fed. Cir. 2008) (public interest favored an injunction despite evidence that the infringing medical product may have been superior).

an injunction where "the public can obtain the products from" the patentee). Natera is not capacity constrained because it has invested in commercial expansion to support the future adoption of its products and has significant commercial capabilities to market and supply Signatera. Malani Dec. ¶¶89-92, 180. Natera has "a broad distribution channel," is "well positioned for scale," has "[c]ommercial teams fully built to support increased future adoption," and is "ready to take on more." *Id*., ¶177. It is positioned "to scale up in a very big way." *Id*. ¶179. RaDaR, on the other hand, is a new entrant that represents only a small portion of the market. *Id*. ¶181. Natera can, therefore, meet future market demand if a preliminary injunction is entered. Furthermore, because Natera by far outstrips its competitors in terms of the number of peer-reviewed and validated studies of Signatera's utility in a variety of cancer indications, Signatera would be considered the safer alternative by the relevant medical community.

VI. CONCLUSION

Natera respectfully requests that the Court enter a preliminary injunction enjoining NeoGenomics' infringement.

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CERTIFICATE OF SERVICE

I hereby certify that I caused the foregoing document to be electronically filed with the Clerk of Court using the CM/ECF system, which will give notice of such filing to all attorneys currently of record in the above-captioned case.

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